MAR 0 8 2004 P

PTO/SB/08a (08-03)
Approved for use through 07/31/2006. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Under ti	ner Sperwork Reduction Act of 1995, n	o perso	ns are required to resp	U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERC or respond to a collection of information unless it displays a valid OMB control number				
;	Substitute of form 1449A/PTO			Complete if Known				
				Application Number	10/650,417			
	INFORMATION DISC	CLO	SURE	Filing Date	8/27/2003			
	STATEMENT BY AP	PLI	CANT	First Named Inventor	Bertino et al.			
	(Use as many sheets as ned			Art Unit	1845 /652_			
	·			Examiner Name				
Sheet	1	of	2	Attorney Docket Number	MSK.P-007-DV			

	U.S. PATENT DOCUMENTS								
Examiner	Cite	Document Number	Publication Date	Name of Patentee or	Pages, Columns, Lines, Where				
initials*	No.1	Number-Kind Code ^{2 (I krown)}	MM-DD-YYYY	Applicant of Cited Document	Relevant Passages or Relevant Figures Appear				
		US-							
	L	US-							
		US-							
		US-							
		US-							
,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,		US-							
		US-							
		US-							
		US-							
		US-							
		US-							
		US-							
		US-							
		US-							
		us-							

FOREIGN PATENT DOCUMENTS									
Examiner Initials*	Cite No.¹	Foreign Patent Document Country Code ³ -Number* - Kind Code ³ (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	Τ°			
963		WO 94/24277	10/27/1994	Sloan-Kettering Inst For Cancer Research					
08		WO 97/33988	9/18/1997	Sloan-Kettering Inst. For Cancer Research					

Examiner Signature	Tos	aidha		Date Considered	12	17	OL	<u>†</u>
EXAMINER:	Initial if reference considered	d, whether or not citation is in cor	formance with MPEP 609.	Draw line through	citation if not i	n conform	nance	and no
onsidered. In	clude copy of this form with n	next communication to applicant.	Applicant's unique citation of	designation numbe	r (optional). 2	See Kind	s Code	s of US
TA Datest Da	commonte of wavewweets new a	MARCO ON A SENSE Office the						

PTO Patent Documents at www.upsto.gov or MPEP 901.04. Senter Office that issued the document, by the two-letter code (WIPO Standard ST.3). For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including

USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chlef Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

PTO/SE/08b (08-03)
Approved for use through 06/30/2006. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Under the Paper	WORK REduction Act of 1	995, no perso	ns are requi	red to respond to a collection of in	formation unless it displays a valid OMB control number		
Substitute for t	form 1449B/PTO			Complete if Known			
l				Application Number	10/650,417		
	MATION DIS			Filing Date	8/27/2003		
STATE	MENT BY A	PPLICA	INT	First Named Inventor	Bertino et al.		
				Art Unit	1645 1652		
(U	se as many sheets as r	necessary)		Examiner Name			
Sheet	2	of	2	Attorney Docket Number	MSK.P-007-DV		

NON PATENT LITERATURE DOCUMENTS							
Examiner Initials* Cite No.! Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (bo magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.							
Str		BANERJEE ET AL., Transfection with a cDNA encoding a Ser ³¹ or Ser ³⁴ mutant human dihydrofolate reductase into Chinese hamster ovary and mouse marrow progenitor cells confers methotrexate resistance, Gene, 1994, Page(s) 269-274, Volume 139					
		BANERJEE ET AL., Molecular mechanisms of resistance to antifolates, A review, Acta Biochimica Polonica, 1995, Page(s) 457-464, Volume 42, Number 4					
		DICKER ET AL., Identification and Characterization of a Mutation in the Dihydrofolate Reductase Gene from the Methotrexate-resistant Chinese hamster ovary cell line Pro ⁻³ Mtx ^{RIII} , The Journal of Biological Chemistry, May 15, 1990, Page(s) 8317-8321, Volume 265, Number 14					
		FAN ET AL., Demonstration of Rb-mediated drug sensitivity and growth inhibition by an inducible expression system, AACR Abstract Form, 1995					
		HUANG ET AL., Nonadditivity of Mutational Effects at the Folate Binding Site of <i>Escherichia coli</i> Dihydrofolate Reductase, Biochemistry, 1994, Page(s) 11576-11585, Volume 33					
		LI ET AL., Development of a Retroviral Construct Containing a Human Mutated Dihydrofolate Reductase cDNA for Hematopoietic Stem Cell Transduction, Blood, June 1, 1994, Page(s) 3403-3408, Volume 83, Number 11					
		ROSOWSKY ET AL., 2,4-Diamino-5-substituted-quinaxolines as Inhibitors of a Human Dihydrofolate Reductase with a Site-Directed Mutation at position 22 and of the dihydrofolate reductases from <i>Pneumocystis carinii</i> and <i>Toxoplasma gondii</i> , J. Med. Chem., 1995, Page(s) 745-752, Volume 38					
		SCHWEITZER ET AL., Mutations at Hydrophobic Residues in Dihydrofolate Reductase. In: Chemistry and Biology of Pteridines 1989, Pteridines and Folic Acid Derivatives, Proceedings of the Ninth International Symposium on Pteridines and Folic Acid Derivatives Chemical, Biological and Clinical Aspects, Zurich, Switzerland 1989, Page(s) 760-764. Sep. 3-8, 1989, Edited by HCh. Curtis, S. Chisla and N. Blau					
	;	SCHWEITZER ET AL., Mutations in the Human Dihydrofolate Reductase In: Chemistry and Biology of Pteridines, Pteridines and Folic Acid Derivatives, 1986, Proceedings of the Eighth International Symposium on Pteridines and Folic Acid Derivatives Chemical, Biological and Clinical Aspects, Montreal Canada. June 15-20, 1986, Page(s) 793-797. Edited by: B.A. Cooper and V.M. Whitehead					
18		SCHWEITZER ET AL., Probing the Role of Two Hydrophobic Active Site Residues in the Human Dihydrofolate Reductase by Site-Directed Mutagenesis, J. Biol. Chem., December 5, 1989, Vol. 264, No. 34, Page(s) 20786-20795.	-				

Examiner Signature	T. Saidha	Date Considered	12/	7-106	F

^{*}EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

'Applicant's unique citation designation number (optional). 'Applicant is to place a check mark here if English language Translation is attached. This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.